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Cyclic Bis-Urea Compounds as Gelators for Organic Solvents

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Abstract: The gelation properties of bis-urea compounds derived from optically pure *trans*-1,2-diaminocyclohexane and 1,2-diaminobenzene, with pendant aliphatic, aromatic, or ester groups, as well as the structure of the resulting gels, have been studied by differential scanning calorimetry, infrared spectroscopy, small-angle X-ray diffraction, and electron microscopy. These compounds have been found to be very potent gelators for organic solvents, such as aliphatic and aromatic hydrocarbons, esters, ketones, and alcohols, at concentrations well below 1 (w/v)%. Gelation by these compounds is completely thermoreversible, with melting temperatures up to 120 °C, and many of the gels display thixotropic properties. Even at low concentrations these compounds self-assemble into elongated and very thin fibers, which in turn form a three-dimensional network in the solvent. Infrared studies showed that aggregation is accompanied by the formation of a hydrogen-bonded network between urea moieties, and a single-crystal X-ray structure of one of the compounds showed that in crystals the molecules assemble into one-dimensional chains, which are stabilized by the formation of eight hydrogen bonds between the urea groups and adjacent molecules. The molecular arrangement in gels is most likely very similar to that in the crystal, but the complete elucidation of the molecular arrangement in gels is complicated because aggregation of these compounds is prone to polymorphism. It is concluded that the very efficient aggregation of these molecules and the elongated shape of the fibers most likely arise from the highly anisotropic hydrogen-bonding properties of these molecules, which is due to the presence of two coplanar oriented urea moieties in a single molecule. Since the bis-urea compounds presented in this paper are very easy to synthesize and many structural variations are possible without loss of the gelation ability, they are excellent building blocks for the construction of functional gels.

Keywords: electron microscopy · gels · hydrogen bonds · molecular modeling · self-assembly ·

Introduction

Gelation of organic solvents by low-molecular weight compounds is the subject of increasing attention, not only because of the numerous applications of gels, but in particular because these compounds represent a new class of gelators that exhibit striking properties with respect to self-assembly phenomena.[1, 2] Although many aspects of the mechanism of gelation are unclear and there is wide range of different structures of low-molecular weight gelators, it appears that these compounds have certain features in common. Gelation of the solvent occurs through self-assembly of the gelator molecules into elongated fiberlike structures, which form an entangled network in the solvent. In contrast to macromolecular gels,[3] the fibers consist of infinite arrays of small molecules, solely held together by noncovalent interactions. Despite impressive achievements of supramolecular chemistry in the controlled self-assembly of small molecules,[4, 5] most low-molecular weight gelators so far have been found by serendipity rather than design. The control of gelation phenomena induced by small organic molecules and the design of new gelators are challenging goals. Up to now these studies are often hampered by synthetic difficulties and the lack of knowledge of possible modes of association.

In a different approach one can design new gelators for organic solvents, starting from criteria derived from some common features of known gelators.[6] In a proper design the geometry of the building blocks and the spatial arrangement and nature of the intermolecular noncovalent interactions determine the structure and properties of the supramolecular

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aggregate.[5] A priori knowledge of the possible modes of aggregation of the designed compounds offers a working model with which one can explain the successes and failures of gelation experiments and which allows one to design new gelator molecules. Recently, Hanabusa et al.[7] and our group[8,9] exploited the capacity of urea derivatives to form extended chains of hydrogen bonds[10] in the design of new gelators for organic solvents.[11] In this paper we present the synthesis and properties of cyclic bis-urea gelators derived from 1,2-cyclohexyldiamine, as well as from 1,2-phenyldiamine, along with a first characterization of the gels by X-ray diffraction techniques and electron microscopy. These bis-urea compounds were found to be excellent gelators for a wide variety of organic solvents, and provide therefore versatile building blocks for the development of functional gelators. Large open-network structures with, for instance, recognition sites, photochemical switches, or electron-conducting properties, offer new possibilities in areas such as catalysis, separation and sensor technology, and materials science.[12]

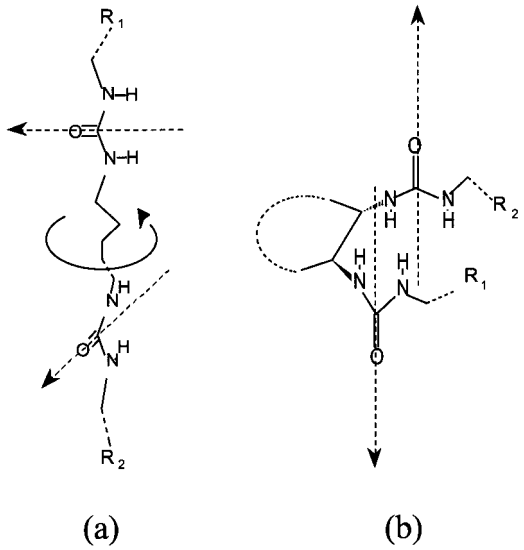

Figure 1. Hydrogen bonding directionality of bis-urea compounds with a flexible linker (a) and with a conformationally constrained linker (b).

Results

Design of new gelators: Previously we found that simple bis-urea compounds, in which the urea groups are connected by a linear alkyl chain, are able to gelate organic solvents and surprisingly, despite their conformational flexibility, aggregate into well-ordered thin flat fibers with lengths up to several hundred micrometers.[8] Structural studies on these fibers indicate that in addition to hydrogen bonding between the urea groups a regular packing of the alkyl chains causes the formation of these well-ordered structures. When the packing of the alkyl chains is distorted as in nonsymmetric bis-urea compounds ($R_1 \neq R_2$) less regular two-dimensional structures are obtained. This behavior can be related to the conformational flexibility of the linker between the two urea moieties making it possible for each urea group to aggregate in a particular direction (Figure 1 a).[13] In order to enforce aggregation along one direction the conformational flexibility of the linker should be reduced and the urea groups should have a coplanar orientation (Figure 1 b). Molecular modeling studies[14, 15] revealed that this can most easily be achieved by using cyclic compounds that are substituted at adjacent positions with urea moieties as a spacer. In the minimum energy conformation of the model compound (*S,S*)-*trans*-1,2-bis(methylureido)cyclohexane the urea groups are rotated out of the plane of the cyclohexyl group and more or less point in opposite directions (Figure 2 a, b). This conformation is stabilized by the presence of a single intramolecular hydrogen bond between the urea groups, which distorts the parallel arrangement of the urea groups (vide infra). A conformational search of the dihedral angles between the cyclohexyl group and both the urea groups identified two other main conformations without an intramolecular hydrogen bond, and which are less stable by 4.8 and 23 kJ mol^{-1}, respectively. In both conformations the urea groups have a coplanar orientation. However, in the first conformation the urea groups point in opposite directions (Figure 2 c, antiparallel conformation), whereas in the least stable conformation the urea groups point

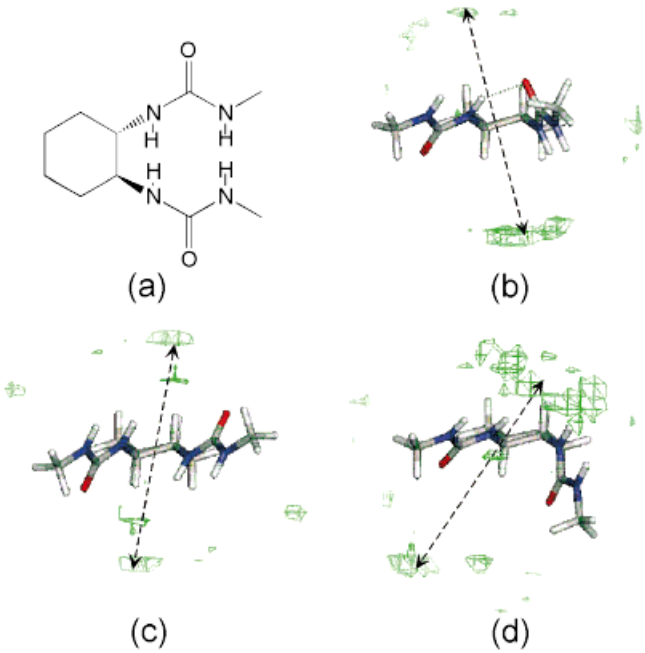

Figure 2. Structure of the model compound *trans*-1,2-bis-(*N*-methylureido)cyclohexane (a), and energy-minimized conformations of *trans*-1,2-bis-(*N*-methylureido)cyclohexane with an intramolecular hydrogen bond between the urea groups (b), and the urea groups oriented antiparallel (c) and parallel (d). The contour levels for an interaction energy of -80 kJ mol^{-1} with a second molecule of 1,2-bis-(*N*-methylureido)cyclohexane are shown in green.

in the same direction (Figure 2 d, parallel conformation). Docking experiments with a second molecule of 1,2-bis(methylureido)cyclohexane revealed that for all three conformations the preferred sites of interaction are located above and below the two urea groups (areas in green in Figure 2). Apparently, noncovalent interactions between these molecules are highly anisotropic, and therefore aggregation along one direction is highly favored over other directions. The line through the most favorable sites of interaction defines the primary axis along which one-dimensional aggregation most

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likely will take place. As one can see from Figure 2, this axis is oriented parallel to the urea carbonyl bonds, and more or less perpendicular to the plane of the cyclohexyl group.

One-dimensional aggregates can be constructed by applying the appropriate symmetry operation along the primary axis.[16] Since *trans*-1,2-bis(methylureido)cyclohexane is chiral, one is limited to the use of a translation or a screw axis operation. In the case of the parallel conformation, both operations will give aggregates that are stabilized by the maximum number of eight hydrogen bonds. However, with the more stable antiparallel conformation or hydrogen-bonded conformation, only a translation operation will give aggregates that are stabilized by eight hydrogen bonds. Molecular modeling revealed that indeed for all four cases the formation of one-dimensional aggregates is strongly favorable by 108–122 kJ mol^{-1} relative to the most stable monomer conformation (Figure 3). In the aggregates the

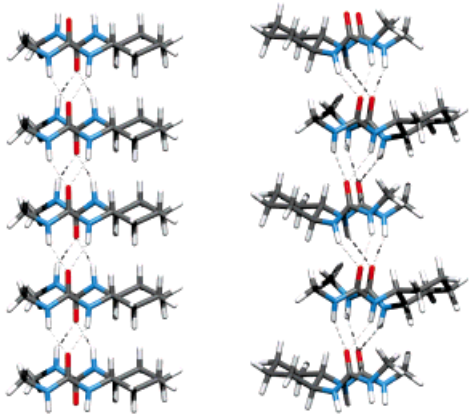
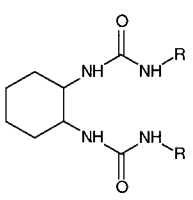


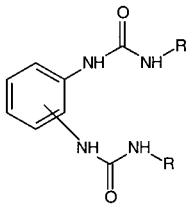
Figure 3. Two possible hydrogen-bonded aggregates of *trans*-1,2-bis-(*N*-methylureido)cyclohexane: a) translational aggregate with urea groups antiparallel, and b) screw axis or glide plane aggregate with urea groups parallel.

molecules are translated by 4.4–4.5 Å, and each molecule forms eight hydrogen bonds with adjacent molecules.[17] Both the intramolecular hydrogen-bonded conformation and the antiparallel conformation give the same translational aggregate shown in Figure 3a, which shows comparable stability to the screw-axis aggregate formed from the parallel conformation (Figure 3b), despite the different stability of the monomeric species. Most interestingly, replacement of the methyl groups on the urea moieties with longer or even branched alkyl chains does not distort the hydrogen-bonding pattern which stabilizes the one-dimensional aggregates.

Molecular modeling experiments with 1,2-bis(methylureido)benzene as a model compound, with the more rigid 1,2-substituted benzene spacer, gave comparable results. Also for this compound the urea groups are rotated out of the plane of the phenyl ring and adopt a more or less coplanar orientation. Again, the conformation with an intramolecular hydrogen bond is more stable than other conformations, in which the urea groups have an antiparallel (+2 kJ mol^{-1}) or a parallel orientation (+22 kJ mol^{-1}). The latter conformation, however, represents a saddle point on the energy surface. Docking experiments with a second molecule of 1,2-bis-(methylureido)benzene revealed highly anisotropic interaction energies, with the primary axis of aggregation oriented parallel to the urea carbonyl bonds. 1,2-Bis(methylureido)benzene is, however, not chiral and therefore less limitations apply for the construction of one-dimensional aggregates than for *trans*-1,2-bis(methylureido)cyclohexane. By starting from the antiparallel conformation of 1,2-bis(methylureido)benzene, application of a translation, glide plane or inversion operation results in one-dimensional aggregates, in which each molecule can form eight hydrogen bonds with adjacent molecules, whereas for the parallel conformation of 1,2-bis(methylureido)benzene such aggregates can be obtained by a translation, a twofold screw axis, or a glide plane. Molecular modeling studies revealed that in all cases stable aggregates are obtained which are 119–127 kJ mol^{-1} more stable than the lowest energy conformation of the monomer. In the aggregates the molecules are translated by 4.5 Å, and each molecule forms eight hydrogen bonds with its neighbors.

Gelation of organic solvents: Starting from these models and encouraged by the preliminary results in our[8, 9] and Hanabusa's laboratories on bis-urea gelators,[7] we prepared a series of cyclohexyl and phenyl bis-urea compounds and investigated their gelating capabilities for organic solvents. Compounds **1**–**11** are readily prepared by reaction of 1,2-diaminocyclohexane or 1,2-diaminobenzene with the corresponding iso-

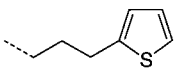


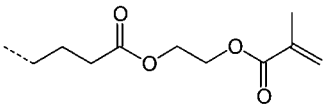


1a (*S*,*S*), R= -$(CH_2)_{11}CH_3$

1b (*R*,*R*), R= -$(CH_2)_{11}CH_3$

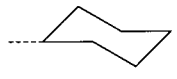
2 (*R*,*R*), R= -$CH(C_2H_5)(CH_2)_3CH_3$

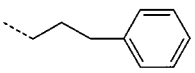
3 (*R*,*R*), R= 

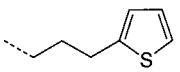
4 (*R*,*R*), R= 

5 (*R*,*S*), R= -$(CH_2)_{11}CH_3$

6 *ortho*, R= -$(CH_2)_{11}CH_3$

7 *ortho*, R= 

8 *ortho*, R= 

9 *ortho*, R= 

10 *meta*, R= -$(CH_2)_{11}CH_3$

11 *para*, R= -$(CH_2)_{11}CH_3$

cyanates. The compounds **1**–**11** are sparingly soluble in most of the solvents investigated, but upon heating at 50–150 °C they gradually dissolve. Upon cooling to room temperature, compounds **1**–**4** and **6**–**9** gelate a wide variety of apolar and polar organic solvents. This process can be repeated many times indicating that gelation is fully thermoreversible. Since preparation of the gels requires heating to temperatures of 50–150 °C, we selected a number of organic solvents with sufficient high boiling point to allow investigation of the gelation phenomena in more detail. The gelation properties and minimum gelation concentrations are compiled in Tables 1 and 2.[18] The cyclohexyl-based compounds are very potent

Table 1. Gelation properties of cyclohexyl bis-urea derivatives.[a]

Solvent	**1**[b]	**2**	**3**	**4**	**5**
hexadecane	< 10	< 2	< 2	p	p
cyclohexane	< 2	< 2	p	< 2	vs
toluene	< 2	< 2	< 10	< 2	vs
p-xylene	< 5	< 2	< 10	< 2	vs
n-butyl acetate	< 10	< 2	p	< 2	p
cyclohexanone	< 2	< 5	< 10	< 2	s
1,2-dichloroethane	< 2	< 2	< 2	< 20	p
dimethyl sulfoxide	< 5	< 10	s	p	p
ethanol	< 2	s	s	p	s
2-propanol	< 2	s	s	p	s

[a] The following abbreviations are used: gelation: g(minimum gelation concentration in mg compound per mL solvent); insoluble at solvent reflux temperature: i; precipitate: p; soluble at room temperature (solubility $> 20\ mg\,mL^{-1}$): s; viscous solution: vs. [b] The same results were obtained for **1a** and **1b**.

gelators for aliphatic and aromatic hydrocarbons, butyl acetate, cyclohexanone, and dichloroethane but, except for compound **1,** are not effective in gelating solvents that strongly compete for hydrogen-bond formation, like the lower alcohols and DMSO.[19] Neither the gelating capability for the different solvents nor the minimum gelation concentrations depend very much on the R group. On the other hand, the *cis* compound **5**, which has the two adjacent urea moieties on the cyclohexyl ring in an axial and equatorial positions (in the chair form) relative to each other, does not gelate any of the solvents investigated. Instead, upon cooling from a hot isotropic solution a viscous solution is formed or the compound slowly precipitates, indicating that aggregation occurs to some extent.

In Table 2 the results of gelation experiments of compound **6**–**11** are summarized. Compounds **6**–**9,** based on *ortho*-substituted bis-ureido-benzene, are potent gelators for a number of organic solvents. Although there are clear differences in solvent compatibility and minimum gelation concentrations, the nature of the R groups does not have dramatic effects on the gelation capability. The *meta*- and *para*-substituted analogues **10** and **11,** on the other hand, failed to gelate any of the solvents investigated (except for **10** with hexadecane). Apparently, the *ortho*-bis-ureido-phenyl moiety is essential for the effective gelation of organic solvents. In this regard there is a strong resemblance with the cyclohexyl-based gelators. In some other aspects there are, however, clear differences between the cyclohexyl-based compounds **1**–**4** and the phenyl-based compounds **6**–**9**. Whereas gels from **1**–**4** can be stored for months without showing any sign of decomposition, gels of **6**–**9** are only stable for a limited period. Depending on the compound, solvent, and concentration these gels slowly precipitate or even start to crystallize after a few days to some weeks. A similar trend is visible when one compares the solvent compatibility and the minimum gelation concentrations of **1**–**4** and **6**–**9** (see Table 1 and 2). The cyclohexyl-based compounds gelate a broader range of solvents and the minimum gelation concentrations are in most cases lower then with the phenyl-based gelators.

Table 2. Gelation properties of phenyl bis-urea derivatives.[a]

Solvent	**6**	**7**	**8**	**9**	**10**	**11**
n-hexadecane	< 2	p	< 10	p	< 2	i
cyclohexane	< 2	i	i	i	p	i
toluene	< 2	< 10	< 2	< 5	p	i
p-xylene	< 2	p	< 5	p	p	i
n-butyl acetate	p	p	p	p	p	i
cyclohexanone	s	< 10	s	s	p	p
1,2-dichloroethane	p	< 2	< 5	< 5	p	i
dimethyl sulfoxide	< 5	s	s	s	p	p
ethanol	p	s	s	s	p	p
2-propanol	s	s	s	s	p	p

[a] For abbreviations see Table 1.

A remarkable feature of many gels of these compounds is that they are thixotropic.[20] When a gel of **1** or **2** is vortexed a viscous liquid is formed, which turns into a gel again after some time. This process can be repeated many times. Gels formed by the cyclohexyl-based gelators **1**–**4** and the phenyl-based gelators **6**–**9** are highly transparent, except for those in hexadecane. Examination by light microscopy shows that the gels are slightly birefringent, but does not reveal more structural details.

Infrared spectroscopy: Aggregation of **1** and **5** in chloroform was further studied by infrared spectroscopy. At low concentration (< 10 mM) for both compounds single sharp absorptions are observed in the NH stretch region and the amide I and II regions. The maxima of these peaks are characteristic for the presence of non-hydrogen-bonded urea groups (Table 3).[21] Increasing the concentration to 20 mM, well above the minimum gelation concentration of 10 mM of **1** in chloroform, causes a shift of the NH and amide I absorptions

Table 3. Infrared spectroscopy of **1** and **5** in chloroform.

Compound	Conc [mM]	λ_{max} [cm^{-1}] NH stretch	Amide I	Amide II
1	10	3360	1651	1564
	30	3327	1632	1589
	74	3327	1632	1591
5	10	3373	1657	1537
	38	3356	1645	1554
	57	3347	1626	1564

towards shorter wavenumbers and a shift of the amide II band towards a higher wavenumber. Similar changes are observed in the infrared spectra of **5** in chloroform, although one has to increase the concentration to 35 mM. These concentration-dependent spectral changes clearly indicate the formation of intermolecular hydrogen bonds between urea groups. Appa-

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rently, both **1** and **5** form hydrogen-bonded aggregates in solution, but only in the case of **1** this also led to gelation of the solvent.

Thermotropic behavior of gels: As noted before, compounds **1**–**4** and **6**–**9** form thermoreversible gels in a wide range of organic solvents. We investigated the thermotropic behavior of *p*-xylene and DMSO gels of **1**, **2**, and **6** in more detail by melting temperature determinations and differential scanning calorimetry (DSC). During heating of the gels, we observed that melting occurred over a broad temperature range. The gels lose their integrity at temperatures 10–25 °C below the temperature at which a clear homogeneous solution was formed. The concentration dependence of the melting temperatures (T_m) of the gels was investigated by the dropping ball method.[22] For all three compounds the *p*-xylene gels melt at 10–30 °C higher temperatures than the DMSO gels, which is in line with the expectation for hydrogen-bonded aggregates.[19] For gels of **2** in *p*-xylene and in DMSO and of **1** and **6** in DMSO a regular increase of the melting temperatures of the gels with increasing concentrations was observed (Figure 4). However, there is no linear correlation between T_m^{-1} and the logarithm of the mole fraction gelator as one would

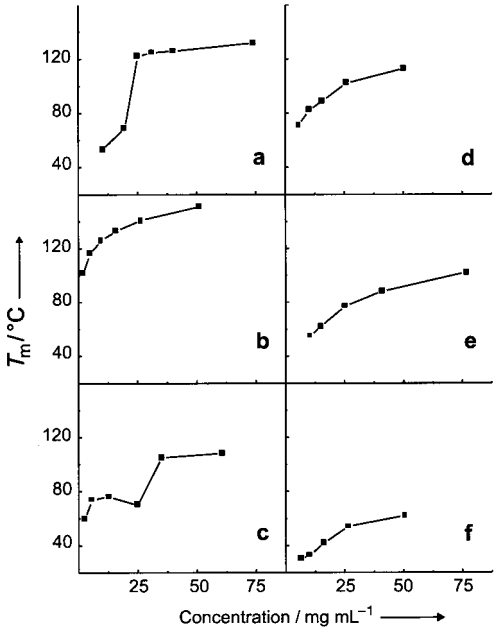

Figure 4. Gel melting temperatures as determined with the dropping ball method for gels of **1** in *p*-xylene (a) and DMSO (d), **2** in *p*-xylene (b) and DMSO (e), and **6** in *p*-xylene (c) and DMSO (f).

expect for the concentration dependence of the melting temperatures for ideal solutions of solids in liquids, and which indeed has been observed for some low molecular weight gel systems.[23]

A remarkable phenomenon was observed for *p*-xylene gels of **1** and **6** at concentrations between 15–20 mg mL^{-1}. For these gels the concentration dependence of T_m shows a strong discontinuity around a concentration of 15–20 mg mL^{-1}. Heating of the gel first causes the ball to drop to the bottom of the vial at 70 °C. At this temperature a slightly turbid viscous solution is formed. Upon further heating, the solution becomes transparent and turns into a gel again at 90–95 °C. For a *p*-xylene gel of **1** a steel ball can be placed again on top of the gel, and heating can be continued until the gel finally melts at 122 °C. For the *p*-xylene gel of **6** we also observed a transition at 90–95 °C to a transparent and very viscous solution, but this was not able to bear a steel ball. Apparently, *p*-xylene gels of **1** and **6** undergo various phase transitions upon heating.

Figure 5 shows the differential scanning calorimetry (DSC) heating and cooling curves of a gel of **1** in *p*-xylene. At 69 °C a strong endothermic transition is observed which occurs over a

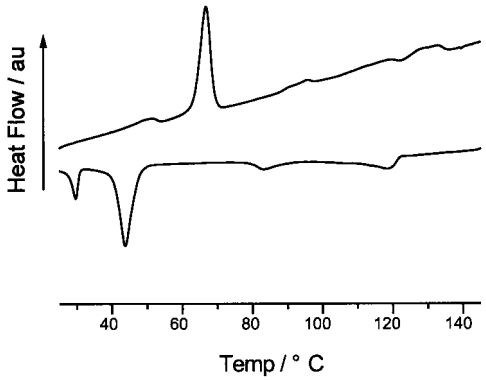

Figure 5. Differential scanning calorimetry heating (upper trace) and cooling (lower trace) scan of a gel of **1** in *p*-xylene. (25 mg mL^{-1}, heating and cooling rate 5 K min^{-1}).

narrow temperature range, pointing to a highly cooperative phase transition. From 87–130 °C a broad endothermic peak occurred which has several maxima, indicating that several processes have taken place. The temperature of the transition at 92 °C agrees very well with the temperature at which the gels become completely transparent. Both the position of the strong transition at 69 °C and the maximum at 92 °C do not depend on the concentration. The high-temperature transition at 115 °C shifts to higher temperature with increasing concentration, and the temperature of this transition correlates well with the melting temperatures of the gels as measured with the dropping ball method. DSC measurements of a DMSO gel of **1** and a *p*-xylene gel of **6** revealed a similar view. For gels of **2** in DMSO and *p*-xylene one broad endothermic transition is only observed during the first heating scan (Table 4). This lack of reversibility is also

Table 4. Thermotropic behavior of gels.[a]

Compound	Solvent	T_m	T_1	T_2	T_3
1	DMSO	102	79 (51)	112 (48)	
	p-xylene	122	69 (40)	92 (3.3)	115 (28)
2	DMSO	77	76 (22)		
	p-xylene	141	123 (20)		
6	DMSO	54	77 (40)		
	p-xylene[b]	108	76 (40)	90 (4.2)	118 (10)

[a] Gels were prepared from 25 mg of the gelating compound and in 1 mL of the solvent. T_m is the melting temperature of the gels as was determined by the dropping ball method. T_1, T_2, and T_3 are the temperatures (in °C) at which the melting endotherms observed with DSC have a maximum. The numbers in parentheses are the enthalpies of the transitions and are given in kJ mol^{-1}. [b] Determined at a concentration of 103 mg mL^{-1}.

observed in crystallization-induced polymer gels and might be due to a large range of crystal imperfection.[24] In this regard it should be noted that **2** is a mixture of diastereomers.

As can be seen in Table 4, for *p*-xylene and DMSO gels of **1**, **2**, and **6** the melting temperatures T_m correspond nicely to T_{max} of the high-temperature transitions as observed by DSC, characterizing the latter as the gel–sol phase transition. The lower temperature transitions observed in gels of **1** and **6** correspond most likely to structural changes of the gels and indicate that gels of **1** and **6** exhibit thermotropic polymorphism.

Small-angle X-ray scattering of gels: The structure of the gels was studied by small-angle X-ray scattering (SAXS) measurements.[25, 26] At low concentrations of the gelating compound (<15 mg mL^{-1} solvent) only a scattering profile was observed, with occasionally in the low-angle region ($1^\circ - 5^\circ$) a very weak Bragg reflection. However, when the concentration of the gelator was increased to 50–100 mg per mL of solvent, several clear Bragg reflections appeared in most of the gels studied (Table 5). Except for a toluene gel of **9**, these

Table 5. Bragg reflections observed in gels.[a]

Compound	Solvent	d_{100} [Å]	d_{200} [Å]	d_{300} [Å]
1	*p*-xylene	32.0	15.5	10.4
2	*p*-xylene	24.0	12.1	–
3	*p*-xylene	22.4	11.5	–
4	*p*-xylene	28.3	–	–
6	*p*-xylene	41.0	19.6	13.0
8	*p*-xylene	24.9	12.0	–
9	toluene	24.6	11.9	13.9[b]

[a] SAXS measurements are done at 25 °C with gels which contain 50–100 mg of the gelating compound in 1 mL of the solvent. [b] This is the (110) reflection, assuming that fibers of **9** have a hexagonal structure.

reflections have a periodicity of 1/1, 1/2, and 1/3. Apparently, gels of these compounds have a lamellar structure.[25] Gels of **1** in cyclohexane or cyclohexanone gave similar SAXS patterns and *d* values as the gel of **1** in *p*-xylene. Apparently, at least for these solvents the molecular packing in aggregates of **1** does not depend on the nature of the solvent. A toluene gel of **9** also showed three low-angle reflections. In this case, however, the reflections have a periodicity of 1/1, $1/\sqrt{3}$, and 1/2, which reveals that compound **9** adopts a hexagonal arrangement[25] in toluene gels.

Thermotropic polymorphism of p-xylene gels of **1** and **6**, as was evident from the DSC measurements, was further investigated by SAXS measurements at different temperatures (Figure 6). For a *p*-xylene gel of **1** only a slight increase of the spacing was observed upon raising the temperature from 20 °C to 60 °C (not shown). At 80 °C, however, well above the first phase transition as observed by DSC, a large shift of the lamellar spacing to a value of 38.4 Å takes place, together with a change of the structure factors of all three reflections. Apparently, a transition to a different lamellar structure has occurred. Upon raising the temperature to 100 °C, above the second phase transition as observed by DSC, a broadening of the 100 reflection was observed together with a shift of its *d* value to 48 Å. Unfortunately,

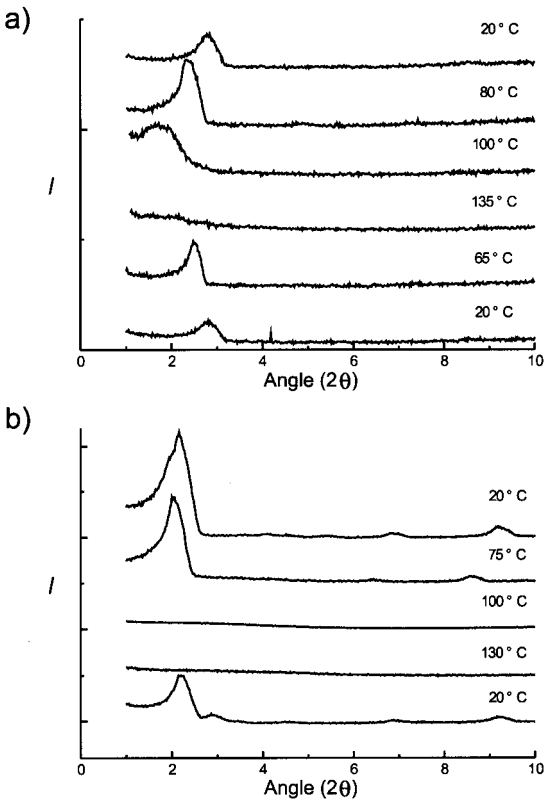

Figure 6. SAXS profiles of concentrated gels of **1** (a) and **6** (b) in *p*-xylene at different temperatures.

we did not observe any higher order reflections and therefore we could not identify the structure. At a temperature of 130 °C, well above the melting temperature of the gel, no Bragg peaks were observed. This observation is consistent with a transition of the ordered gel structure to an isotropic solution. Cooling of this isotropic solution to room temperature resulted in a SAXS pattern almost identical to that of the starting gel, indicating that formation of ordered structures by **1** in *p*-xylene is fully reversible within this temperature and concentration range.

For a *p*-xylene gel of **6** more complicated behavior was observed. At 20 °C a broad reflection with a maximum at 40.9 Å and at the low-angle edge a shoulder was observed, together with a number of weak reflections between 3° and 10°. We were not able to assign these reflections by assuming that a single structure is present. At 75 °C, well above the first phase transition as observed by DSC, the pattern greatly simplified. A strong first-order reflection together with three weak higher order reflections were observed, with a periodicity of 1/1, 1/2, 1/3, and 1/4. Apparently, a lamellar structure is formed with the spacing amounting to 43.8 Å. At 100 °C, well above the second phase transition as measured by DSC, no clear reflections were observed, indicating that structures with a clear long-range order are no longer present. Cooling the sample from 130 °C to room temperature, led to the appearance of strong first-order reflections together with three weak higher order reflections, which have a periodicity characteristic for a lamellar structure. In addition, one more first-order reflection was observed at a *d* value of 41.8 Å.

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Single-crystal X-ray structure of 9: Although electron microscopy and X-ray diffraction do not give sufficient information to elucidate the packing in the fibers on the molecular level, it is clear that these bis-urea compounds self-assemble into highly ordered structures. All attempts to obtain single crystals from **1**–**8** suitable for X-ray analysis failed. However, compound **9**, which has modest gelation properties compared to **1**–**8** (see Tables 1 and 2), crystallizes from polar solvents like ethanol. Single-crystal x-ray analysis revealed the molecules to be in a conformation with the urea groups in a parallel orientation (Figure 7a). The angle between the least-square

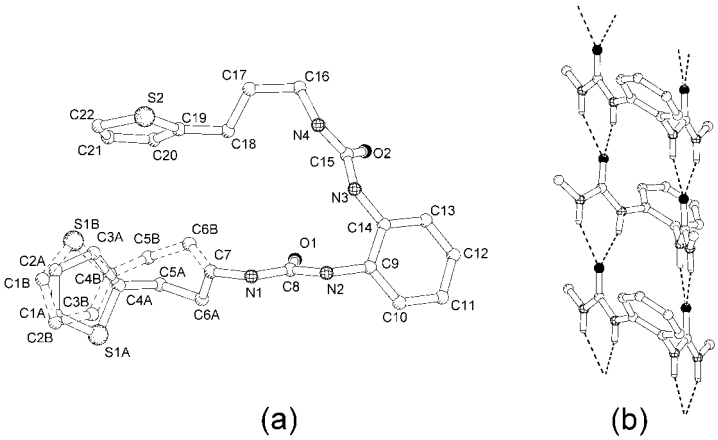

Figure 7. a) PLUTON plot of the molecular structure of **9**, as obtained from the X-ray crystal structure determination. Hydrogen atoms are omitted for clarity. The minor disorder component is drawn with dashed bonds. b) Hydrogen-bonded chain, running parallel to the *c* axis. Thiophene groups, part of the propyl groups, and the hydrogen atoms not involved in hydrogen-bonding have been omitted for clarity.

planes through the urea groups containing C8 and C15 and the least-square plane through the linking phenyl group amounts to 67.6(5)° and 40.7(5)°, respectively. The thiophene group and two atoms of the linking propyl group are disordered over two positions.

The main packing motif is a one-dimensional chain of molecules, running parallel to the crystallographic *c* axis (Figure 7b). Four N–H···O hydrogen bonds link two adjacent molecules, which are related by a crystallographic glide operation. The donor–acceptor distances lie in the range 2.753(12)–3.067(9) Å; the N–H···O angles vary between 146.5(5)° and 153.4(6)°. The conformational disorder in the thienyl–propyl moiety does not disturb the hydrogen-bond interactions.

Interestingly, this crystal structure does not account for the low-angle reflections observed in toluene gels of this compound. Compound **9** crystallizes in spacegroup *Cc*, which shows a systematic absence of the 010 reflection. If the molecular arrangement in gels of **9** was the same as in the crystal structure, the first observable reflection in the low-angle region would have been the 020 reflection at 15.04 Å. In gels, however, a strong reflection was observed at 24.6 Å (vide supra). Apparently, the molecular arrangement in a toluene gel of **9** is different from that in crystals obtained in polar solvents.

Electron microscopy: The morphology of gels in various solvents was investigated by electron microscopy. Figure 8 shows some electron micrographs of the cyclohexyl-based gelators and the phenyl-based gelators in an aromatic solvent. In the gel state we observed for both type of compounds long thin fibers, which form an entangled network. The regular shape and the extreme aspect ratio of the fibers must arise from a strong anisotropic growth process, indicating that the fibers have a well-ordered molecular packing. From the electron micrographs in Figure 8 it is clear that structural differences between the compounds have a large effect on the morphology. Compound **1** forms in *p*-xylene untwisted thin straight fibers. On the other hand, the observation of many bends indicates that these fibers are highly flexible (Figure 8a). Fibers formed by **2** in *p*-xylene have a less regular

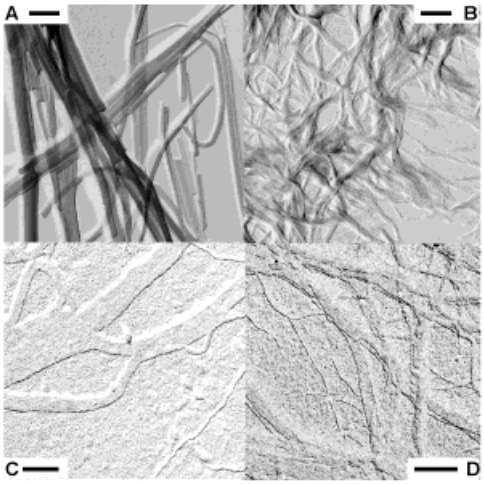

Figure 8. Electron micrographs of **1a** in *p*-xylene (A, 3 mg mL^{-1}, Pt shadow 45°, bar = 500 nm), **2** in *p*-xylene (B, 3 mg mL^{-1}, Pt shadow 45°, bar = 500 nm), **6** in *p*-xylene (C, 3 mg mL^{-1}, Pt shadow 10°, bar = 100 nm), and **8** in toluene (D, 3 mg mL^{-1}, Pt shadow 10°, bar = 200 nm).

structure than fibers of **1** and are strongly twisted (Figure 8b). Both types of fibers are flat and consist of stacks of smaller flat fibers. The diameter of the smallest entities which can be distinguished is 30–50 nm for **1** and 15–25 nm for **2**, which is an order of magnitude larger than the molecular dimensions of **1** and **2**. Compound **6** and **8** also form fiberlike structures, but they have a very different appearance (Figure 8c and 8d). Many very thin fibers can be distinguished on the micrographs, with diameters as small as 2–4 nm, which are comparable to the molecular dimensions of **6** and **8**. Numerous spots are visible on the micrographs where small fibers fuse with others to form sheets. These sheets stack into layered structures. From the shadow length the thickness of a single sheet is calculated to be approximately 3–5 nm for **6** and **8**.

Figure 9 shows electron micrographs of gels of compound **1** in different solvents. From the micrographs it is clear that a change in the solvent has a large effect on the morphology of the fibers. However, X-ray diffraction on gels of **1** gives the same spacing of 31.5 Å in cyclohexanone and *p*-xylene (vide supra). Apparently, despite their different shapes the fibers shown in Figure 9 have the same molecular arrangement.

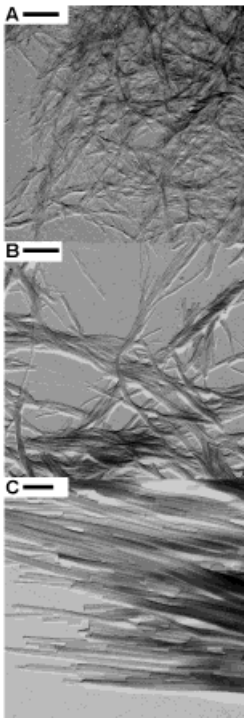

Figure 9. Electron micrographs of **1a** in cyclohexane (A, 3 mg mL^{-1}, Pt shadow 45°, bar = 500 nm), in cyclohexanone (B, 3 mg mL^{-1}, Pt shadow 45°, bar = 500 nm), and in toluene (C, 3 mg mL^{-1}, Pt shadow 45°, bar = 500 nm).

Therefore the different morphologies should originate from differences in interfacial free energy or attachment energies in the various solvents.[27] However, we do not observe a clear correlation between the fiber morphology and solvent properties like polarity, polarizability, or hydrogen-bonding capability.

The chirality of the gelator molecules is an intriguing aspect in view of their organization in self-assembled aggregates. The cyclohexyl-based bis-urea gelators **1**–**4** have two stereogenic centers but rather to our surprise, the chirality is hardly expressed at the supramolecular level.[5, 28] Of the solvents compiled in Table 1, only for gels in ethanol a clear twist of fibers is observed in the electron micrographs. Thus, for *(S,S)*-**1a** right-handed helices are observed, and for *(R,R)*-**1b** left-handed helices are observed (Figure 10). Apparently, the

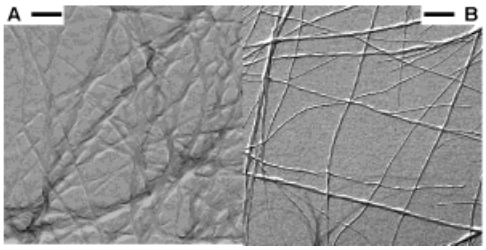

Figure 10. Electron micrographs of **1a** in ethanol (A, 3 mg mL^{-1}, Pt shadow 45°, bar = 200 nm) and of **1b** in ethanol (B, 3 mg mL^{-1}, Pt shadow 45°, bar = 500 nm).

screw-sense of the helices is related to the handedness of the molecules. The pitch of the helices however, is not regular. This indicates that the twists do not arise from a helical arrangement at the molecular level, but more likely are the result of the anisotropy of the interfacial energy.[29]

Fibers of both type of compounds form an entangled network. Many intertwined and fused fibers are observed in the micrographs in Figure 8–10. Similar structural features are often observed in gels of (bio)polymers as junction zones, stabilizing the network through specific interactions between fibers.[30] It has been argued that thixotropy is related to reversible disruption and formation of junction zones.[20, 33] Their presence might therefore explain the thixotropic behavior of gels of **1**–**4** and **6**–**9**. Interestingly, we did not observe any fused or intertwined structures in gels of linear bis-urea compounds.[8] It should be emphasized that gels of these linear bis-urea compounds are not thixotropic and are easily and irreversible destroyed by mechanical agitation.

Discussion

In this study we have examined the gelation capability of a series of bis-urea compounds, as well as the structure and properties of gels formed by these compounds. It was found that compounds **1**–**4** and **6**–**9** are potent gelators for a wide range of organic solvents. In solution these compounds self-assemble into long fiberlike structures, most likely through hydrogen bond formation between the urea groups. The fibers form a three-dimensional network in the solvent, thereby turning the solution into a gel. A comparison of the structures of the highly gelating compounds, that is **1**–**4** and **6**–**9**, shows that these compounds only have in common that the urea groups are connected by a *trans*-1,2-substitued cyclohexyl and an *ortho*-substituted phenyl ring, respectively. Many different substituents on the urea groups are allowed without loss of the gelating capability. On the other hand, compounds **5**, **10**, and **11** do not gelate any of the solvents investigated. The infrared studies showed that also these compounds aggregate through hydrogen bond formation between the urea groups. They differ, however, from **1**–**4** and **6**–**9** by the substitution pattern of the two urea groups on the bridging ring system. Apparently, the spatial arrangement of the urea groups in the *trans*-1,2-bis(ureido)cyclohexyl and 1,2-bis(ureido)phenyl moieties is essential for the gelating capability of these compounds. Molecular modeling studies showed that in these moieties the two urea groups are rotated out of the plane of the carbocyclic connector and adopt a coplanar orientation. In such a conformation the hydrogen bonding groups are directed along a common axis. Self-assembly of these compounds through multiple intermolecular hydrogen bonding leads therefore to one-dimensional aggregates, similar to the hydrogen-bonded arrays of **9** in crystals of this compound.

In gels, **1**–**4** and **6**–**9** do not form crystals, but instead form a network of very long and thin fibers. The optical micrographs of the fairly dilute systems studied in this paper show a weakly birefringent plain texture without structural details. Such a texture can be explained by the presence of many fibrous structures, each fiber having a well-defined molecular arrangement, but macroscopically the fibers are randomly oriented. This conclusion is further substantiated by, for example, the results obtained from DSC, SAXS, and electron

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microscopy measurements. The electron micrographs of gels of **6** and **8** clearly show that these compounds form thin strands of only 2–4 nm thick, which is comparable to the molecular length of these molecules. Most likely, these small strands consist of only one to three arrays of **6** and **8**, each of which is stabilized by hydrogen bonds between the urea groups along a direction parallel to the long axis of the strands. This conclusion is further supported by the fact that structures with a very regular shape and high aspect ratio must arise form a strong anisotropic growth process. Most likely, the formation and shape of fibers in gels are governed by similar principles to those which determine the shape and formation of the crystals.[32, 33] In crystallization processes the growth rate of a crystal plane increases with the attachment energy for that plane, resulting in crystal morphologies that are dominated by the crystal faces with the lowest attachment energies.[27] Similarly, elongated structures like fibers will be formed as the tips of the fibers are the fastest growing interfaces, indicating that intermolecular interactions in a direction perpendicular to the tip of the fibers are much stronger than the interactions along other directions. Most likely, the urea groups of the gelator molecules are exposed at the fast growing tips and, as a consequence, the gelator molecules are oriented with the urea groups parallel with the long molecular axis of the fibers. Indeed, in needle-shaped crystals of **9** the crystal growth has taken place along the crystallographic *c* axis, parallel to hydrogen-bonded chains of urea groups.

The SAXS measurements showed that many of the gels have a lamellar structure. For gels **6** and **8** the spacing of the lamella is 41 Å and 24.9 Å, respectively, which nicely corresponds to the thickness of these sheets (2–4 nm) as has been estimated from the electron micrographs (Figure 8C and D). These electron micrographs further revealed that the sheets consist of strands of these compounds, with the long axis of the strands parallel to the fiber long axis. Most likely, the lamellar structures in gels of the other compounds also consist of closely packed hydrogen-bonded arrays of bis-urea gelators. Within such an arrangement, however, different molecular packings are possible, as the SAXS measurements of **6** and **9** provide clear evidence of polymorphism. Polymorphism can be related to different packings of strands of the gelator molecules, for example in a rectangular lattice or a hexagonal lattice, but it can also be the result of different arrangements of the bis-urea gelator molecules in each strand. For instance, in crystals of **9**, the two urea moieties in each molecule have a parallel orientation, and the hydrogen-bonded aggregate is built up by a glide plane. Molecular modeling, however, revealed that other arrangements, that is translational or screw aggregate of the parallel conformation of the 1,2-bis(ureido)benzene moiety, or aggregates built up from the antiparallel conformation of 1,2-bis(ureido)benzene through translation or inversion operations, are equally stable within a window of 8 kJ mol^{-1}. For compounds **6**–**9**, based on the data presented in this paper, we cannot determine which of these arrangements dominate in gels of these compounds, and probably two or more of these structures coexist in gels.

For the 1,2-bis(ureido)cyclohexane-based gelators **1**–**4** the number of possible arrangements is limited, because these molecules are chiral and nonracemic. Therefore aggregates can only be constructed by application of translation or screw axis operations. Molecular modeling studies showed that translational aggregates built up from molecules with the urea groups in an antiparallel conformation and screw axis constructed from molecules with the urea groups in a parallel conformation are equally stable (see Figure 3). Two possible lamellar arrangements of molecules of **1** are depicted in Figure 11. In the translational aggregate, hydrogen bonding

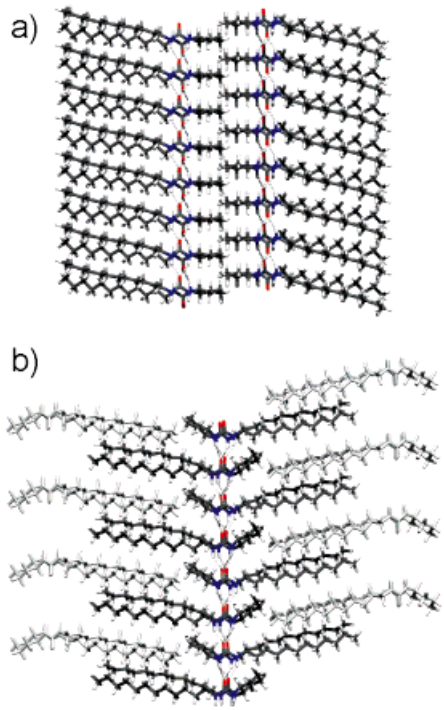

Figure 11. Tentative arrangement of **1** in a double layer structure, constructed from translational aggregates (a), and an intercalated layer structure constructed from screw axis aggregates (b).

between the two 1,2-bis(ureido)cyclohexane moieties allows close packing of the alkyl chains (Figure 11a). For the screw axis aggregate this is not the case, and close packing of the alkyl chains can only be achieved through intercalation (Figure 11b). The experimentally found spacing of lamella of **1** (31.5 Å), however, fits neither with a single layer structure nor with the intercalated structure. A more likely arrangement of molecules of **1** in lamella is a double layer structure (Figure 11a). In such an arrangement a tilt of the molecules can explain the discrepancy between the theoretical thickness of 42 Å and the experimentally determined spacing of 31.5 Å. An alternative structure might be a double layer of **1**, in which the molecules are bent, but other arrangements are also possible.

The DSC and SAXS measurements at different temperatures revealed a striking resemblance in the thermotropic polymorphism of gels of **1** and **6**. Gels of both compounds show a strong cooperative phase transition at 60–70 °C to a second lamellar phase. These observations suggest that this transition involves melting of the alkyl chains to a less ordered packing, analogous to the main bilayer phase transitions

observed in lamellar phases of lipids.[34] This hypothesis is supported by the observation that compound **2,** in which the dodecyl chains are replaced by branched alkyl chains, does not display other phase transitions than melting of the gels. Another remarkable difference in the gelation capability of **1** and **6** and the other gelators is that only **1** and **6** form gels with polar solvents, whereas the other bis-urea compounds dissolve in these solvents. Apparently, the packing forces of the alkyl chains in **1** and **6** compensate for the hydrogen bond breaking capacity of polar solvents.

In gels of **1** and **6** a second cooperative phase transition occurs at approximately 90 °C. For gels of **6** this transition involves most likely a disintegration of the double layer structure into much smaller assemblies of strands of **6**, as no long-range order is present. For gels of **1** an ordered structure is still present, but unfortunately the SAXS data provide insufficient information to identify this phase. The remarkable change in optical and viscoelastic properties indicate, however, that a major reorganization of strand and/or network structure has occurred.

In conclusion, starting from molecules which preferentially self-assemble in one dimension, we have succeeded in the design of new gelators for organic solvents. The derivatives of 1,2-bis(ureido)benzene and *trans*-1,2-bis(ureido)cyclohexane presented herein are very potent gelators for a wide range of organic solvents. Although the morphology of the fibrous network within the gels depends both on the nature of the substituents on the urea groups and on the solvent, the molecular arrangement of these bis-urea compounds is dominated by intermolecular hydrogen bond formation between the urea moieties. These one-dimensional strands of hydrogen-bonded bis-urea compounds assemble into sheets and lamella, which in turn stack into fiberlike structures. To what extent this secondary assembly process has taken place is determined by the interfacial energy of the strands, which mainly depends on the nature of the substituents and on the solvent. As a result, these bis-urea compounds display a rich variety of morphologies.

The bis-urea compounds presented have many properties in common with other gelators. They are, however, very easy to synthesize, and many structural variations are possible without losing the gelating ability. For these reasons, the bis-urea compounds are not only excellent model compounds to study gelation phenomena in more detail, but also are excellent building blocks for the development of functional gels. Research along these lines is in progress.

Experimental Section

Materials and methods: Solvents for synthesis were purified and dried when necessary according to standard procedures. (*S,S*)- and (*R,R*)-1,2-cyclohexyldiamine was purchased from Fluka, and dodecylisocyanate was obtained from Acros. The diamines and isocyanates were purified by Kugelrohr distillation prior to use unless noted otherwise. The solvents for gelation experiments were of analytical grade and used as received. NMR spectra were recorded on either a Varian VXR-300 spectrometer operating at 300 MHz for ^{1}H or 75 MHz for ^{13}C, or on a Varian Gemini 200 NMR spectrometer operated at 200 MHz for ^{1}H or 50 MHz for ^{13}C. Chemical shifts are denoted in δ units relative to the solvent and converted to the TMS scale using 7.26 (76.91) for $CDCl_3$ and 2.49 (39.50) for [D_6]DMSO (the numbers in brackets denote solvent chemical shifts for ^{13}C). The splitting patterns in the ^{1}H NMR spectra are described as follows: s (singlet), d (doublet), dd (double doublet), t (triplet), m (multiplet), br (broad). IR spectra were recorded on a Mattson Instruments Series 4020 FTIR spectrometer. Elemental analysis were performed by J. Ebels, H. Draaijer, and J. Hommes in the microanalytical department of the University of Groningen.

(−)-(*S,S*)-Dodecyl-3-[2-(3-dodecyl-ureido)cyclohexyl]urea (**1a**): A solution of dodecylisocyanate (3.17 g, 15 mmol) in toluene (20 mL) was slowly added to a solution of (*S,S*)-1,2-cyclohexyldiamine (0.8 g, 7 mmol) in toluene (100 mL). The reaction mixture, which immediately became viscous, was stirred for 16 h at room temperature and 2 h at 100 °C. After cooling to room temperature, the gel-like reaction mixture was filtered (glassfilter G4) to give a white waxy solid. The waxy solid was stirred for 16 h with CH_2Cl_2 (50 mL) and collected by filtration. This procedure was repeated with diethyl ether. Finally, the white solid was dried for 6 h at 60 °C under vacuum (1 mm Hg pressure). Yield: 99 % (3.73 g, 6.9 mmol); m.p. 235 °C (decomp); $[\alpha]_D = -0.067$ ($c = 1$, ethanol/$CHCl_3$ 1/1 v/v); ^{1}H NMR (300 MHz, $CDCl_3$, 60 °C): $\delta = 4.94$ (d, $J = 6.6$ Hz, 2H), 4.40 (t, $J = 5.3$ Hz, 2H), 3.45 (br, 2H), 3.10 (m, 4H), 2.04 (d, $J = 12.1$ Hz, 2H), 1.72 (br m, 2H), 1.46 (br m, 4H), 1.28 (br, 40H), 0.89 (t, $J = 6.6$ Hz, 6H); ^{13}C NMR (75.48 MHz, $CDCl_3$, 60 °C): $\delta = 159.2$ (s), 55.0 (d), 40.7 (t), 33.5 (t), 31.9 (t), 30.4 (t), 29.6 (t), 29.5 (t), 29.3 (t), 27.1 (t), 25.2 (t), 22.6 (t), 13.9 (q); IR ($CHCl_3$): $\tilde{\nu} = 3360$, 1651, 1564 cm^{-1}; $C_{32}H_{64}N_4O_2$ (536.88): calcd. C 71.60, H 12.00, N 10.40; found C 71.63, H 12.51, N 10.47.

(+)-(*R,R*)-Dodecyl-3-[2-(3-dodecyl-ureido)cyclohexyl]urea (**1b**): This compound was synthesized as described above for **1a**, starting from dodecylisocyanate (2.75 g, 13 mmol) and (*R,R*)-1,2-cyclohexyldiamine (0.7 g, 6.1 mmol). Yield: 65 % (2.12 g, 4 mmol); m.p. 235 °C (decomp); $[\alpha]_D = +0.069$ ($c = 1$, ethanol/$CHCl_3$ 1/1 v/v); ^{1}H NMR (300 MHz, $CDCl_3$, 60 °C): $\delta = 5.07$ (d, $J = 6.6$ Hz, 2H), 4.55 (t, $J = 5.3$ Hz, 2H), 3.45 (br, 2H), 3.10 (m, 4H), 2.04 (d, $J = 12.1$ Hz, 2H), 1.72 (br m, 2H), 1.45 (br m, 4H), 1.28 (br, 40H), 0.89 (t, $J = 6.6$ Hz, 6H).

(±)-3-Heptylisocyanate: To a cooled solution (0 °C) of sodium azide (10 g) in water (50 mL), 2-ethylhexanoyl chloride (16.5 g, 100 mmol) dissolved in acetone (20 mL) was added at such a rate that the temperature of the reaction mixture was kept below 10 °C. After stirring for 40 min at 0 °C, the reaction mixture was extracted with ice-cold toluene (50 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and heated at 80 °C for 3 h. The solvent was removed under vacuum and the liquid residue was purified by bulb-to-bulb distillation (70 °C, 15 mm Hg). Yield 67 % (9.9 g, contains approximately 8 mol % toluene); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.37$ (m, 1H), 1.65 – 1.30 (m, 8H), 0.99 (t, $J = 7.5$ Hz, 3H), 0.92 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (75.48 MHz, $CDCl_3$): $\delta = 57.8$, 36.1, 29.8, 28.3, 22.3, 13.9, 10.4; IR (neat): $\tilde{\nu} = 2270$ cm^{-1}.

(*R,R*)-3-Heptyl-3-[2-(3-(3-heptyl)-ureido)cyclohexyl]urea (**2**): This compound was prepared as described above for **1a**, starting from (±)-3-heptylisocyanate (1.9 g, 14 mmol) and (*R,R*)-1,2-cyclohexyldiamine (0.58 g, 5.1 mmol). Yield: 83 % of a mixture of diastereomers (1.67 g, 4.2 mmol); m.p. 230 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$, 60 °C): $\delta = 5.12$ (d, $J =$ 22.3 Hz, 2H), 4.23 (br, 2H), 3.44 (br, 4H), 2.07 (d, $J = 9.9$, 2H), 1.69 (br, 2H), 1.30 (br m, 20H), 0.88 (m, 12H); ^{13}C NMR (75.48 MHz, $CDCl_3$, 60 °C): $\delta = 158.7$ (s), 55.03 (d), 54.8 (d), 54.5 (d), 51.9 (d), 51.8 (d), 51.7 (d), 34.9 (t), 34.8 (t), 33.4(t), 28.5 (t), 28.4 (t), 28.2 (t), 28.1 (t), 24.5 (t), 22.7 (t), 13.9 (q), 10.2 (q), 9.9 (q); IR (KBr): $\tilde{\nu} = 1633$, 1585 cm^{-1}; $C_{22}H_{44}N_4O_2$ (396.61): calcd. C 66.60, H 11.22, N 14.10; found C 66.56, H 11.29 N 14.07.

Monomethyl succinoyl chloride: Succinic anhydride (30 g, 300 mmol) was suspended in methanol (200 mL) and refluxed for 2 h. The solvent was removed in vacuo and a white solid was obtained. ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.60$ (t, 2H), 2.61 (t, 2H), 3.65 (s, 3H); ^{13}C NMR (50.32 MHz, $CDCl_3$): $\delta = 28.4$ (t), 28.7 (t), 51.8 (q), 172.8 (s), 178.2 (s). The crude monoester was dissolved in dichloromethane (150 mL). Thionyl chloride (25 mL, 345 mmol) and DMF (3 drops) were added and the resulting mixture was refluxed for 2 h. Solvent and unconverted thionyl chloride were evaporated in vacuo and the residual liquid was submitted to bulb-to-bulb distillation (80 °C/10 mm Hg) yielding 41.2 g of a colorless liquid (274 mmol, 91 %). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 3.68$ (s, 3H), 3.19 (t, 2H, $J = 6.6$ Hz), 2.65 (t, 2H, $J = 6.6$ Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$): $\delta = 172.9$ (s), 171.3 (s), 52.0 (q), 41.6 (t), 29.0 (t); IR (neat): $\tilde{\nu} = 1796$, 1740 cm^{-1}.

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Methyl 3-oxo-4-(2-thienyl)butanoate: This synthesis was based on a literature procedure.[35] Thiophene (10.1 g, 120 mmol) was dissolved in dichloromethane (150 mL) and monomethyl succinoylchloride (19.6 g, 130 mmol) was added. The mixture was stirred until a homogeneous solution was obtained and subsequently cooled to 0 °C by means of an ice/water bath. Then $SnCl_4$ (32.6 g, 125 mmol) was added at such a rate that the temperature of the reaction mixture remained below 15 °C. During the addition the mixture turned from yellow to dark red. The reaction mixture was stirred overnight and poured into ice/dilute HCl. The resulting slurry was stirred until the salts were dissolved. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with a dilute aqueous $NaHCO_3$ solution, water, and brine and dried on anhydrous $MgSO_4$. After filtration the solvent was removed in vacuo, yielding a dark oil. The oil was submitted to bulb-to-bulb distillation (100–120 °C/0.02–0.05 mm Hg) to yield 19.8 g of a colorless liquid (99.9 mmol, 83 %). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.77$ (dd, 1H, $J = 3.9$ Hz, $J = 0.9$ Hz), 7.65 (dd, 1H, $J = 4.9$ Hz, $J = 0.9$ Hz), 7.14 (dd, 1H, $J = 3.9$ Hz, $J = 4.9$ Hz), 3.70 (s, 3H), 3.27 (t, 2H, $J = 6.8$ Hz), 2.77 (t, 2H, $J = 6.8$ Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$): $\delta = 190.8$ (s), 172.9 (s), 143.4 (s), 133.5 (d), 131.8 (d), 128.0 (d), 33.7 (t), 27.8 (t); IR (neat): $\tilde{\nu} = 1765$, 1738 cm^{-1}.

4-(2-thienyl)butanoic acid: Methyl 3-oxo-4-(2-thienyl)-butanoate ester (11.7 g, 59.0 mmol) was dissolved in ethyleneglycol (125 mL). Hydrazine monohydrate (20 mL , 412 mmol) was added and the mixture was stirred at 60 °C (bath temperature) for 0.5 h. Subsequently KOH (13.5 g, 241 mmol) was added and the temperature of the mixture was raised to 150 °C (bath temperature). This temperature was maintained for 1 h, after which the reaction vessel was equipped with a Dean–Stark trap and the temperature raised to 190 °C (bath temperature). In total 7 mL of water was removed. The mixture was kept at reflux for 3 h, allowed to cool to room temperature, and poured into ice/dilute HCl. A white suspension formed immediately. The suspension was extracted with ethyl acetate. The ethyl acetate layer was washed with water and brine and dried on anhydrous $MgSO_4$. The solvent was evaporated in vacuo and the residual oil submitted to bulb-to-bulb distillation (105 °C/0.03 mm Hg), to yield 8.29 g of a colorless liquid (48.7 mmol, 83 %). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.14$ (dd, 1H, $J = 5.1$ Hz, $J = 1.1$ Hz), 6.93 (dd, 1H, $J = 3.3$ Hz, $J = 5.1$ Hz), 6.82 (dd, 1H, $J = 3.3$ Hz, $J = 1.1$ Hz), 2.91 (t, 2H, $J = 7.3$ Hz), 2.43 (t, 2H, $J = 7.3$ Hz), 2.02 (quintet, 2H, $J = 7.3$ Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$): $\delta = 179.9$ (s), 143.8 (s), 126.8 (d), 124.6 (d), 123.3 (d), 33.0 (t), 28.9 (t), 26.4 (t); IR (cm^{-1}): $\tilde{\nu} = 1707$ neat.

4-(2-thienyl)butanoyl chloride: 4-(2-Thienyl)-butanoic acid (8.29 g, 48.7 mmol) was dissolved in dichloromethane (50 mL). Thionyl chloride (4.4 mL, 60.6 mmol) was added and the mixture was stirred overnight. A little darkening of the solution had occurred. Solvent and excess thionyl chloride were removed in vacuo and the residual dark liquid was purified by bulb-to-bulb distillation (80 °C/0.06 mm Hg) to yield 7.71 g of a colorless liquid (40.8 mmol, 84 %). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.18$ (dd, 1H, $J = 5.1$ Hz, $J = 1.1$ Hz) 6.97 (dd, 1H, $J = 5.1$ Hz, $J = 3.3$ Hz), 6.84 (dd, 1H, $J = 3.3$ Hz, $J = 1.1$ Hz), 2.96 (t, 2H, $J = 7.3$ Hz), 2.94 (t, 2H, $J = 7.3$ Hz), 2.10 (quintet, 2H, $J = 7.3$); ^{13}C NMR (50.32 MHz, $CDCl_3$): $\delta = 173.4$ (s), 142.8 (s), 126.9 (d), 124.9 (d), 123.6 (d), 45.8 (t), 28.2 (t), 26.8 (t); IR (neat): $\tilde{\nu} =$ 1798 cm^{-1}.

3-(2-thienyl)propylisocyanate: Sodium azide (6.51 g, 0.1 mol) was dissolved in water (150 mL) and the solution was cooled by means of an ice/water bath to 0 °C. A solution of 4-(2-Thienyl)-butanoylchloride (7.71 g, 40.8 mmol) in acetone (75 mL) was added dropwise to the sodium azide solution at such a rate that the temperature remained below 10 °C. After addition was complete, the mixture was stirred for another 30 min. Then the solution was extracted with cold toluene (ca. 0 °C). The toluene layer was washed with brine and dried on anhydrous $MgSO_4$ for 10 min. During this period some gas evolution already occurred. The solution was filtered and heated while stirring on an oil bath at 100 °C until gas evolution had stopped. The solvent was evaporated in vacuo and the residue submitted to bulb-to-bulb distillation (80 °C/0.1 mm Hg) to yield 5.53 g of a colorless liquid (33.1 mmol, 81 %). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.17$ (dd, 1H, $J = 5.1$ Hz, $J = 1.0$ Hz), 6.96 (dd, 1H, $J = 3.4$ Hz, $J = 5.1$ Hz), 6.84 (dd, 1H, $J = 3.4$ Hz, $J = 1.0$ Hz), 3.37 (t, 2H, $J = 6.4$ Hz), 2.97 (t, 2H, $J = 7.3$ Hz), 2.00 (quintet, 2H, $J = 6.4$ Hz, $J = 7.3$ Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$): $\delta =$ 143.0 (s), 126.8 (d), 124.7 (d), 123.4 (d), 41.8 (t), 32.7 (t), 26.5 (t); IR (neat): $\tilde{\nu} = 2278$ cm^{-1}.

(*R*,*R*)-(3-(2-Thienyl)propyl)-3-[2-(3-(3-(2-thienyl)propyl)ureido)cyclohexyl]urea (3): This compound was prepared as described above for **1a**, starting from *(R,R)*-1,2-cyclohexyldiamine (0.3 g, 2.6 mmol) and 3-(2-thienyl)propylisocyanate (0.71 g, 5.25 mmol). Yield 0.61 g of a white powder (61 %, 1.6 mmol); m.p. 244 °C (d); ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = 7.14$ (d, 2H, $J = 4.8$ Hz), 6.78 (dd, 2H, $J = 4.8$, $J =$ 3.3 Hz), 6.68 (d, 2H, $J = 3.3$ Hz), 5.85 (t, 2H, $J = 5.7$ Hz), 5.59 (d, 2H, $J = 6.2$ Hz), 3.09 (br s, 2H), 2.85 (dt, 4H, $J = 5.7$ Hz, $J = 6.2$ Hz), 2.61 (t, 4H, $J = 7.5$ Hz), 1.72 (d, 2H, $J = 11.7$ Hz), 1.53 (quintet, 4H, $J = 6.2$ Hz, $J =$ 7.5 Hz,), 1.46 (m, 2H), 0.92–1.10 (m, 4H); ^{13}C NMR (75.48 MHz, [D$_6$]DMSO): $\delta = 158.0$ (s) 144.3 (s), 126.6 (d), 124.1 (d), 123.1 (d), 102.4 (d), 53.0 (t), 38.6 (t), 32.8 (t), 32.0 (t), 26.4 (t), 24.2 (t); IR (nujol mull): $\tilde{\nu} = 1632$, 1589 cm^{-1}.

Butanedioic acid mono 2-(methacryloyloxy)ethyl ester: Succinic acid anhydride (7.68 g, 77 mmol), methacrylic acid glycol ester (10 g, 77 mmol) and 4-methoxyphenol as inhibitor (0.1 g) were stirred at 90 °C for 18 h. After cooling to room temperature an opaque viscous oil was obtained. Yield 17.68 g (100 %, 77 mmol). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 6.1$ (s, 1H), 5.6 (m, 1H), 4.4 (s, 4H), 2.7 (m, 4H), 1.9 (m, 3H); ^{13}C NMR (50.32 MHz, $CDCl_3$): $\delta = 174.9$ (s), 172.1 (s), 166.7 (s), 135.6 (s), 126.0 (t), 62.1 (t), 62 (t), 28.6 (t), 28.5 (t), 17.9 (q).

Methacrylic acid 2-(3-chlorocarbonyl-propionyloxy)ethyl ester: A solution of butanediodic acid mono 2-(methacryloyloxy)ethyl ester (5.02 g, 22 mmol), oxalyl chloride (9 mL, 100 mmol), and a few crystals of 4-methoxyphenol as inhibitor in dichloromethane (150 mL) was stirred overnight at room temperature. The solvent and excess of oxalyl chloride were removed in vacuo yielding 5.47 g of a pale yellow oil (100 %, 22 mmol). ^{1}H NMR revealed that the product was nearly pure and the crude product was therefore used in the next step without further purification. An analytical sample was obtained by bulb-to-bulb distillation (colorless oil, 135 °C, 0.08 mmHg). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 6.13$ (s, 1H), 5.6 (m, 1H), 4.36 (s, 4H), 3.22 (t, $J = 6.6$ Hz, 2H), 2.71 (t, $J = 6.6$ Hz, 2H), 1.9 (s, 3H); ^{13}C NMR (50.32 MHz, $CDCl_3$): $\delta = 173.9$ (s), 170.6 (s), 166.7 (s), 135.6 (s), 126.1 (t), 62.6 (t), 62.0 (t), 41.4 (t), 28.9 (t), 18.0 (q); IR (neat): $\tilde{\nu} =$ 1790, 1739, 1722, 1637 cm^{-1}.

Methacrylic acid 2-(3-isocyanato-propionyloxy)ethyl ester: A cold solution of methacrylic acid 2-(3-chlorocarbonyl-propionyloxy)ethyl ester (3.7 g, 15 mmol) was dropwise added to a solution of sodium azide (1.54 g, 24 mmol) in water (20 mL), while maintaining the temperature below 10 °C by cooling with an ice-bath. After stirring for 1 h at 0–10 °C the acid azide was isolated from the reaction mixture by extraction with cold toluene (50 mL). After drying over anhydrous $MgSO_4$ and addition of 4-methoxyphenol (50 mg), the toluene solution was stirred for 12 h at 70–80 °C. The reaction mixture was allowed to cool to room temperature and was concentrated at reduced pressure to yield 2.48 g of a pale orange oil. According to ^{1}H NMR the crude product consisted for 83 w/w % of the isocyanate (yield 60 %, 9.1 mmol). The remaining 17 w/w % was toluene. An analytical sample was obtained by bulb to bulb distillation (colorless oil, 125 °C, 0.007–0.010 mm Hg). All attempts to purify the larger amounts of the product by distillation resulted in polymerization of the product. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.13$ (s, 1H), 5.60 (m, 1H), 4.38 (s, 4H), 3.60 (t, $J = 6.2$ Hz, 2H), 2.63 (t, $J = 6.2$ Hz, 2H), 1.95 (s, 3H); ^{13}C NMR (50.32 MHz, $CDCl_3$): $\delta = 170.4$ (s), 166.9 (s), 135.7 (s), 126.0 (t), 62.4 (t), 62.0 (t), 38.3 (t), 35.2 (t), 18.0 (q); IR (neat): $\tilde{\nu} =$ 2227, 1739, 1722, 1637 cm^{-1}.

(1*R*,2*R*)-1,2-bis-[3-(2-(2-(methacyloyloxy)ethoxycarbonyl)ethyl)ureido]-cyclohexane (4): This compound was prepared as described for **1a,** starting from *(1R,2R)*-(−)-1,2-cyclohexyldiamine (0.35 g, 3.1 mmol) and methacrylic acid 2-(3-isocyanatopropionyloxy)ethyl ester (2.1 g, contains 7.7 mmol isocyanate). Methoxyphenol (50 mg) was added as an inhibitor. Yield 1.68 g of a white solid (93.5 % based on the cyclohexyldiamine, 2.9 mmol); m.p. 190 °C (decomp); $[\alpha]_D = 1.5$ ($c = 1$, DMSO); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.03$ (s, 2H), 5.51 (s, 2H), 5.16 (m, 4H), 4.26 (m, 8H), 3.30 (m, 6H), 2.43 (t, $J = 6.22$ Hz, 4H), 1.92 (d, $J = 11.7$ Hz, 2H), 1.84 (s, 6H), 1.6 (d, $J = 7.3$ Hz, 2H), 1.15 (m, 4H); ^{13}C NMR (75.48 MHz, [D$_6$]DMSO): $\delta = 172.9$ (s), 167.68 (s), 159.15 (s), 136.89 (s), 127.42 (t), 63.70 (t), 63.06 (t), 54.16 (d), 36.58 (t), 36.05 (t), 34.15 (t), 34.12 (t), 25.63 (t), 19.22 (q); IR (KBr): $\tilde{\nu} =$ 3310, 1726, 1631, 1591, 1535 cm^{-1}; $C_{26}H_{40}N_4O_{10}$ (568.63): calcd. C 54.92, H 7.09, N 9.85, O 28.14; found C 54.61, H 7.18, N 9.87, O 28.53.

(1*R*,2*S*)-Dodecyl-3-[2-(3-dodecyl-ureido)-cyclohexyl]urea (**5**): This compound was prepared as described for **1a**, starting from (*1R,2S*)-cyclohexyldiamine (0.65 g, 5.7 mmol) and dodecylisocyanate (2.41 g, 11.4 mmol). Yield 1.92 g of a white powder (63%, 3.6 mmol); m.p. 96 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.10$ (br s, 2H), 4.62 (br s, 2H), 3.79 (br s, 2H), 3.13 (m, 4H), 1.75 (br s, 2H), 1.47 (br s, 12H), 1.25 (br s, 34H), 0.88 (t, $J = 6.6$ Hz, 6H); ^{13}C NMR (75.48 MHz, $CDCl_3$): $\delta =$ 159.3 (s), 50.1 (d), 40.3 (t), 31.9 (t), 30.5 (t), 29.7 (t), 29.65 (t), 29.6 (t), 29.4 (t), 27.2 (t), 22.7 (t), 14.1 (q); IR (nujol mull), $\tilde{\nu} = 3316$, 1640, 1539 cm^{-1}; $C_{32}H_{64}N_2O_4$ (536.84): calcd. C 71.59 H 12.02 N 10.44; found C 71.59 H 11.87 N 10.45.

Dodecyl-3-[2-(3-dodecylureido)phenyl]urea (**6**): This compound was prepared as described for **1a**, starting from 1,2-diaminobenzene (0.44 g, 4.07 mol) and dodecylisocyanate (1.73 g, 8.2 mmol). The product was purified by repeated precipitation from hot toluene. Yield 1.41 g of a white powder (65%, 2.66 mmol); m.p. 184 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = 7.65$ (br s, 2H) 7.43 – 7.48 (m, 2H), 6.93 – 6.97 (br s, 2H), 6.25 (br s, 2H), 3.07 (d, 4H, $J = 5.9$ Hz), 1.40 – 1.50 (br s, 4H), 1.20 – 1.40 (br s, 36H), 0.86 (br s, 6H); ^{13}C NMR (75.48 MHz, [D$_6$]DMSO): $\delta = 155.5$ (s), 131.4 (s), 123.1 (d), 122.7 (d), 39.0 (t), 30.8 (t), 29.3 (t), 28.5 (t), 28.3 (t), 28.1 (t), 26.0 (t), 21.5 (t), 13.3 (q); IR (nujol): $\tilde{\nu} = 1645$, 1576 cm^{-1}; $C_{32}H_{58}N_4O_2$ (530.83): calcd. C 72.40, H 11.00, N 10.60; found C 71.86, H 11.03, N 10.50.

Cyclohexyl-3-[2-(3-cyclohexylureido)phenyl]urea (**7**): This compound was prepared as described for **1a**, starting from 1,2-diaminobenzene (0.56 g, 5.22 mmol) and cyclohexylisocyanate (1.34 g, 10.7 mmol). Yield 1.71 g of a white powder (91%, 4.77 mmol); m.p. 204 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = 7.65$ (s, 2H) 7.46 (dd, 2H, $J = 3.7$ Hz, $J = 5.5$ Hz), 6.91 (dd, 2H, $J = 3.7$ Hz, $J = 5.5$ Hz), 6.40 (d, 2H, $J = 7.3$ Hz), 3.44 (m, 2H), 1.81 (br d, 4H, $J = 10.3$ Hz), 1.66 (m, 4H), 1.54 (m, 2H), 1.09 – 1.34 (m, 10H); ^{13}C NMR (75.48 MHz, [D$_6$]DMSO): $\delta = 155.0$ (s), 131.4 (s), 123.2 (d), 122.8 (d), 48.0 (d), 33.0 (t), 25.2 (t), 24.4 (t); IR (nujol): $\tilde{\nu} = 1624$, 1587 cm^{-1}; $C_{20}H_{30}N_4O_2$ (358.48): calcd. C 67.00, H 8.40, N 15.60; found C 66.58, H 8.46, N 15.39.

4-Phenylbutanoyl chloride: 4-Phenylbutanoic acid (8.59 g, 52.3 mmol) was suspended in dichloromethane (50 mL). Thionyl chloride (6.0 mL, 83 mmol) was added and the mixture was refluxed for 3 h. The solvent and excess thionyl chloride were removed in vacuo and the residual oil was submitted to bulb-to-bulb distillation (90 °C/0.1 mm Hg), yielding 9.08 g of a colorless liquid (49.7 mmol, 95%). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta =$ 7.19 – 7.40 (m, 5H), 2.92 (t, 2H, $J = 7.2$ Hz), 2.72 (t, 2H, $J = 7.4$ Hz), 2.07 (quintet, 2H, $J = 7.2$ Hz, $J = 7.4$ Hz); ^{13}C NMR (50.32 MHz, $CDCl_3$): $\delta =$ 173.7 (s), 140.4 (s), 128.6 (d), 128.4 (d), 126.4 (d), 46.1 (t), 34.2(t), 26.4 (t); IR (neat): 1797 cm^{-1}.

3-Phenylpropylisocyanate: Sodium azide (6.5 g, 0.1 mol) was dissolved in water (100 mL) and cooled to ca. 0 °C by means of an ice/water bath. Under vigorous stirring, a solution of 4-phenylbutanoyl chloride (9.08 g, 49.7 mmol) in acetone (75 mL) was added at such a rate that the temperature of the reaction mixture remained below 15 °C. A white solid precipitated immediately. After addition was complete, the reaction mixture was stirred for another 30 min. Then the solution was extracted with cold toluene (0 °C). The toluene layer was washed with brine and dried on anhydrous $MgSO_4$ for 10 min. During this period some gas evolution already occurred. After filtration of the mixture, the solution was stirred at 100 °C until the evolution of nitrogen gas had ceased. The solvent was evaporated and the residue submitted to bulb-to-bulb distillation (85 °C/ 0.1 mm Hg) yielding 6.25 g of a colorless liquid (38.8 mmol, 78%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.32 – 7.36$ (m, 2H), 7.21 – 7.25 (m, 3H), 3.33 (t, 2H, $J = 6.6$ Hz), 2.75 (t, 2H, $J = 7.5$ Hz), 1.95 (quintet, 2H, $J = 6.6$ Hz, $J =$ 7.5 Hz); ^{13}C NMR (70.48 MHz, $CDCl_3$): $\delta = 140.5$ (s), 128.5 (d), 128.4 (d), 126.1 (d), 42.1 (t), 32.6 (t), 32.5 (t),; IR (neat): $\tilde{\nu} = 2275$ cm^{-1}.

(3-Phenylpropyl)-3-[2-(3-(3-phenylpropyl)ureido)phenyl]urea (**8**): This compound was prepared as described for **1a**, starting from 1,2-diaminobenzene (0.31 g, 2.86 mmol) and 3-phenylpropylisocyanate (0.94 g, 5.83 mmol). During the synthesis of this compound in chloroform, a clear and transparent gel was formed. In order to drive the reaction to completion, more solvent was added and the reaction mixture was refluxed for 1h. Yield 0.97 g of a white powder (2.26 mmol, 79%); m.p. 181 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = 7.79$ (s, 2H), 7.46 – 7.49 (m, 2H), 7.14 – 7.29 (m, 10H), 6.94 – 6.97 (m, 2H), 6.57 (t, 2H, $J = 5.5$ Hz), 3.08 (dt, 4H, $J = 5.5$ Hz, $J = 5.9$ Hz), 2.60 (t, 4H, $J = 7.7$ Hz), 1.73 (quintet, 4H, $J =$ 7.7 Hz, $J = 5.9$ Hz); ^{13}C NMR (75.48 MHz, [D$_6$]DMSO): $\delta = 155.9$ (s), 141.7 (s), 131.6 (s), 128.2 (d), 125.6 (d), 123.5 (d), 123.1 (d) 38.9 (t), 32.5 (t), 31.5 (t); IR (nujol mull): $\tilde{\nu} = 1643$, 1577 cm^{-1}; $C_{26}H_{30}N_4O_2$ (430.54): calcd. C 72.50, H 7.00, N 13.00; found C 72.56, H 7.05, N 12.95.

(3-(2-Thienyl))-3-[2-(3-(3-(2-thienyl)propyl)ureido)phenyl]urea (**9**): This compound was prepared as described for **1a**, starting from 1,2-diaminobenzene (0.33 g, 3.05 mmol) and 3-(2-thienyl)propylisocyanate (0.84 g, 6.21 mmol). During the synthesis of this compound in chloroform, a clear and transparent gel was formed. In order to drive the reaction to completion, more solvent was added and the reaction mixture was refluxed for 1 h. After cooling the mixture to room temperature, the solvent was removed in vacuo, and the product was purified by crystallization from ethanol. Yield 0.95 g of colorless needles (2.50 mmol, 82%); m.p. 178 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = 7.78$ (s, 2H), 7.46 (dd, 2H, $J = 5.9$ Hz, $J = 1.0$ Hz), 7.30 (dd, 2H, $J = 5.1$ Hz, $J = 1.0$ Hz), 6.91 – 7.00 (m, 4H), 6.86 (dd, 2H, $J = 5.1$ Hz, $J = 5.9$ Hz), 6.60 (t, 2H, $J = 5.5$ Hz), 3.12 (dt, 4H, $J =$ 6.8 Hz, $J = 5.5$ Hz), 2.82 (t, 4H, $J = 7.6$ Hz), 1.76 (quintet, 4H, $J = 6.8$ Hz, $J = 7.6$ Hz); ^{13}C NMR (75.48 MHz, [D$_6$]DMSO): $\delta = 156.3$ (s), 144.6 (s), 131.9 (s), 127.2 (d), 124.8 (d), 123.8 (d), 123.5 (d), 39.0 (t), 32.1 (t), 26.8 (t); IR (nujol mull): $\tilde{\nu} = 1632$, 1591 cm^{-1}; $C_{22}H_{32}N_4O_2S_2$ (448.64) calcd: C 59.70, H 5.90, N 12.70% found: C 59.68, H 5.90, N 12.53.

Dodecyl-3-[3-(3-dodecylureido)phenyl]urea (**10**): This compound was prepared as described for **1a**, starting from 1,3-diaminobenzene (0.39 g, 3.61 mmol) and dodecylisocyanate (1.55 g, 7.33 mmol). Yield 1.04 g of a white powder (54%, 1.96 mmol); m.p. 177 – 181 °C; ^{1}H NMR (300 MHz, 120 °C, [D$_6$]DMSO): $\delta = 8.12$ (s, 1H), 7.44 (s, 1H), 6.91 – 7.04 (m, 3H), 5.91 (t, 2H), 3.06 (dt, 4H), 1.20 – 1.50 (m, 42H), 0.86 (t, 6H). Due to the high temperatures required in order to keep **10** in solution, excessive line broadening occurred. Therefore, coupling constants could not be obtained. ^{13}C NMR (75.48 MHz, 120 °C, [D$_6$]DMSO): $\delta = 154.7$ (s), 140.4(s), 127.9 (d), 110.6 (d), 107.4 (d), 39.0 (t), 30.7 (t), 29.4 (t), 28.4 (t), 28.2 (t), 28.0 (t), 25.9 (t), 21.4 (t), 13.1 (q); IR (nujol mull): $\tilde{\nu} = 1631$, 1575 cm^{-1}; $C_{32}H_{58}N_4O_2$ (530.83): calcd. C 72.40, H 11.00, N 10.60; found C 72.30, H 11.02, N 10.56.

Dodecyl-3-[4-(3-dodecylureido)phenyl]urea (**11**): A solution of dodecylisocyanate (2.30 g, 10.9 mmol) in dichloromethane (20 mL) was added to a solution of 1,4-diaminobenzene (0.58 g, 5.36 mol) in dichloromethane (20 mL). A white precipitate was formed immediately. After stirring for 1 h the precipitate was collected by filtration and washed with dichloromethane and diethylether. The product was characterized by means of ^{1}H NMR and ^{13}C NMR and appeared to be 1-amino-4-(3-dodecylureido)-benzene. Yield 1.69 g of a white powder (99%, 5.29 mmol); m.p. 146 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.80$ (s, 1H), 6.79 (d, 2H), 6.43 (d, 2H), 5.84 (t, 1H), 4.65 (s, 2H), 3.00 (dt, 2H), 1.36 (br s, 2H), 1.23 (br s, 18H), 0.84 (t, 3H); ^{13}C NMR (75.48 MHz, $CDCl_3$): $\delta = 155.7$ (s), 143.3 (s), 129.7 (s), 120.2 (d), 114.1 (d), 39.1 (t), 31.3 (t), 29.9 (t), 29.1 (t), 29.0 (t), 28.8 (t), 28.7 (t), 26.4 (t), 22.1 (t), 14.0 (t); IR (nujol mull): $\tilde{\nu} = 1626$, 1574 cm^{-1}.

1-Amino-4-(3-dodecylureido)benzene (1.69 g, 5.29 mmol) was dissolved in refluxing toluene (50 mL) under an atmosphere of nitrogen and dodecylisocyanate (1.13 g, 5.35 mmol) was added. Refluxing was continued for 2 h after which the reaction mixture was allowed to room temperature. After filtration 2.48 g of a white solid was isolated (88%, 4.67 mmol); m.p. > 250 °C (decomp); ^{1}H NMR (300 MHz, 120 °C, [D$_6$]DMSO): $\delta = 7.81$ (s, 2H), 7.20 (s, 4H), 5.75 (t, 2H), 3.08 (dt, 4H), 1.20-1.50 (m, 42H), 0.87 (t, 6H); Due to the high temperatures required in order to keep **11** in solution, excessive line-broadening occurred. Therefore, coupling constants could not be obtained. ^{13}C NMR (75.48 MHz, 120 °C, [D$_6$]DMSO): $\delta = 155.7$ (s), 127.5 (s), 118.3 (d), 39.1 (t), 31.3 (t), 29.9 (t), 29.1 (t), 29.0 (t), 28.8 (t), 28.3 (t), 26.0 (t), 21.5 (t), 13.9 (t); IR (nujol): $\tilde{\nu} = 1622$, 1572 cm^{-1}; $C_{32}H_{58}N_4O_2$ (530.83): calcd. C 72.40, H 11.00, N 10.60; found C 72.14, H 10.89, N 10.49.

Gelation experiments: In a typical gelation experiment a weighed amount of the bis-urea compound and 1 mL of the solvent were placed in a test tube, which was sealed and then heated until the compound dissolved. The solution was allowed to cool to room temperature. Gelation was considered to have occurred when a homogeneous substance was obtained, which exhibited no gravitational flow. For the determination of the melting points a steel ball (150 mg) was placed on top of the gel and the vial was sealed. A series of these samples was placed in a stirred oil bath which was slowly heated (typically 2 – 4 °C min^{-1}), while the positions of the steel balls were observed and the temperature was simultaneously monitored with the aid of a thermocouple in one of the vails. The melting point of a particular

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sample was taken as the temperature at which the steel ball reached the bottom of the vial.

Differential scanning calorimetry: A given amount of gel was placed in a preweighed pan, which was sealed and weighed on a six-decimal place balance. Heating and cooling scans were measured on a Perkin-Elmer DSC 7 instrument at a scan rate of 5 °C min^{-1}. After the measurements the pan was weighed again to check for possible leakage.

Electron microscopy: For electron microscopy a piece of the gel was placed on a formvar/carbon-coated copper grid (400 mesh) and removed after one min, leaving some small patches of the gel on the grid. After the specimens had been dried at low pressure ($>10^{-5}$ Torr), they were shadowed at an angle of 10° or 45° with platinum. The specimens were examined in a JEOL 1200 EX transmission electron microscope operating at 80 kV. In studying the specimens, we first searched for patches of the gel to be sure that the observed structures originate from the gel. Micrographs were taken from structures at the periphery of the gel patches because here the fibers are deposited in a layer thin enough to be observed by transmission electron microscopy.

Small-angle X-ray diffraction: For X-ray diffraction measurements a glass capillary with a diameter of 1 mm (wall thickness 0.01 mm) was filled with a concentrated gel (50–75 mg bis-urea compound per mL solvent) and sealed with a torch. X-ray diffractograms were recorded on a Philips powder diffractometer in $\theta/2\theta$ geometry, using $Cu_{K\alpha1/K\alpha2}$ radiation (1.54060 Å and 1.54439 Å), from 1° to 10° in 0.02° steps.

Crystal structure determination of 9: $C_{22}H_{26}N_4O_2S_2$, $M_r = 442.61$, colorless, needle shaped crystal ($0.13 \times 0.10 \times 075$ mm^3), monoclinic, spacegroup *Cc* (no. 9) with $a = 9.879(3)$, $b = 30.075(4)$, $c = 8.910(3)$ Å, $\beta = 123.23(2)°$, $V = 2214.4(12)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.3276(7)$ g cm^{-3}, $F(000) = 936$, $\mu(Mo_{K\alpha}) = 2.7$ cm^{-1}. A total of 12630 reflections were measured, 3901 independent, ($1.36° < \theta < 26.5°$, ω scan, $T = 150$ K, $Mo_{K\alpha}$ radiation, graphite monochromator, $\lambda = 0.71073$ Å) on a Enraf–Nonius CAD4 Turbo diffractometer with a rotating anode. Data were corrected for Lp effects and for linear instability of the reference reflections, but not for absorption. The structure was solved by automated direct methods (SHELXS86). Refinement on F^2 was carried out by full-matrix least-square techniques (SHELXL-93); no observance criterion was applied during refinement. The thiophene group containing S1 displayed conformational disorder for which a two-site disorder model was introduced; the site occupation factor of the major component refined to 0.755(6). Mild bond length restraints were applied to enforce equal bond lengths and bond angles in both disorder components. Hydrogen atoms were included in the refinement at calculated positions riding on their carrier atoms. All ordered non-hydrogen atoms were refined with anisotropic displacement parameters; hydrogen atoms were refined with a fixed isotropic displacement parameter related to the value of the equivalent isotropic displacement parameter of their carrier atoms. Refinement converged at final w$R2$ value of 0.251, $w = 1/[\sigma^2(F^2) + (0.10P)^2]$, where $P = (\mathrm{Max}(F_o^2, 0) + 2(F_c^2)/3$, $R1 = 0.090$ (for 1956 reflections with $I > 2\sigma(I)$), $S = 0.96$, for 263 parameters. A final Fourier showed no residual density outside -0.46 and 0.49 e Å^{-3}.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-113747. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Molecular modeling: Molecular modeling calculations were done using CHARMm 23 as implemented in Quanta96 from Molecular Simulations Incorporated. All calculations were done in the gas phase with a dielectric constant of 1 and with non-bonded cut-off range of 15 Å, with a switch function operating from 11 Å to 14 Å. Symmetry-averaged dipole preserving electrostatic potential derived point charges from AM1 optimized structures were used.

For calculation of the interaction maps one molecule was placed at the center of a cubic box of $15 \times 15 \times 15$ Å^3 and with grid points spaced by 0.5 Å. A second molecule was placed on a grid point and rotated with 60° increments around the Euler angles, and the interaction energy was calculated for each rotation step. This procedure was repeated for each grid point, after which the interaction map was constructed from the most favorable interaction energies at each grid point.

For the evaluation of the aggregate stability, one-dimensional aggregates were constructed by using the crystal modeling facility of Quanta96, by placing along one axis three symmetry-related copies both in positive and negative directions and each spaced by 5 Å, whereas for the other two axes the image molecules were placed at 500 Å, that is a distance much larger than the cut-off distance. This assembly was then used as the starting point for a full-geometry optimization, including the cell constants.

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